REMARKS

The present claims have been rejected by Examiner as follows:

1. Claims 1-3, 5-8, and 10-13 are rejected as unpatentable over Yamamoto and Nagpal. The Board has affirmed the first ground of rejection, but denominated it as a new ground of rejection under 37 CFR § 1.196 (b).

In an earlier appeal, the Board has affirmed that Examiner has successfully made a prima facie case of obviousness. While Applicant does not agree with this allegation, this issue will not be dealt with further herein, but Applicant reserves the right to revisit this issue on further appeal, if necessary.

In the previous response, Applicant pointed out the unexpected results reported in the specification of the application as filed. Examiner has responded "Applicant's argument was considered but not persuasive for the following reasons." Applicants provide evidence and arguments herein which show that Examiner's reasons were erroneous, and that the results presented in the specification are in fact unexpected.

Examiner has alleged that the reasoning previously presented by the Applicant in showing unexpected results is flawed, charging that "in order to argue unexpected and/or unobvious results, the amount of corticosteroid in each case has to be kept constant." Applicants respectfully respond that this is incorrect. It is generally known in the art that the potency of a corticosteroid is based upon the performance of said steroid in a vasoconstriction assay. The potency of the corticosteroid is assigned according to the particular formulation in which it is contained. Thus, the 1% hydrocortisone acetate formulation used in the patent specification is considered to be low-potency at a concentration of 1% in the vehicle it is administered. The same is true for 0.05% alcometasone dipropionate being a medium-potency corticosteroid and 0.1% betamethasone valerate being a high-potency corticosteroid. The whole point of assigning potency to a corticosteroid formulation is to indicate the activity of that

formulation, and thus treatment a particular condition is determined according to the assigned potencies of the various corticosteroid formulations. It is known in the art that corticosteroid potency correlates very well with efficacy in the treatment of psoriasis. For example, Cornell and Stoughton carried out a study to determine the correlation between the vasoconstrictor assay (the test for potency) and the clinical activity in psoriasis (Arch Dermatol vol 121, Jan 1985, pp. 63-67. An excerpt from the abstract is reproduced below:

> Excellent correlation between the vasoconstriction assay and selected paired comparison studies occurred in 20 of 23 instances...vasoconstrictor assay is an inexpensive and reliable method for screening glucocorticosteroid formulations for clinical activity in psoriasis.

Thus, prima facie, a person of ordinary skill in the art will assume that a higher potency corticosteroid formulation will be more effective in treating psoriasis.

Referring to Example 1, and the accompanying Figures 2, it is clear that the combination of tazarotene and an high potency corticosteroid are surprisingly more efficacious than the other combinations tested, having a clear improvement over the other combinations virtually from the onset of the administration until reaching an advantage of about 15% over the next best treatment from 4 days until the end of the study. Figure 1 also shows a clinically significant reduction in plaque elevation for the tazarotene/high-potency corticosteroid combination compared to the other treatments. The Board stated that "the combination and tazarotene and a low-potency corticosteroid appear to provide better results than the combination of tazarotene and a mid-potency corticosteroid in reducing the severity of psoriasis in patients over a period of 12 weeks." According to the Board's observation, increasing the potency of the corticosteroid has no apparent advantage in combinations up to mid-potency corticosteroids. Based upon this, a person of ordinary skill would not expect that further increasing the potency of the corticosteroid would be beneficial. In fact, based upon the Board's observation that the mid-potency corticosteroid appears

to be less efficacious in combination with tazarotene as compared to the low potency corticosteroid, one of ordinary skill might expect a high potency corticosteroid to reduce the efficacy of the treatment even further. Therefore, it is surprising that the combination of tazarotene and a high-potency corticosteroid should have such a significant improvement over the other treatments. Essentially, the results presented in the specification point to an ideal combination—that of a high potency corticosteroid and tazarotene—where a person of ordinary skill would not expect such an ideal combination to exist based upon the results for the low and mid potency combinations.

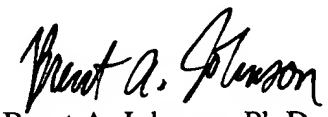
Furthermore, it is generally accepted in the art that increasing the potency of a medication also increases the incidence of adverse events. If that were not the case, the maximum potency for a medication would be used in most cases. As pointed out in the previous response, in the present application increasing the potency of the corticosteroid actually unexpectedly decreased the number of adverse events. In the Decision on Appeal, the Board alleged that using a high-potency corticosteroids does not appear to reduce side effects, as Applicant has maintained. Applicants submit herewith a reference by Gollnick (British Journal of Dermatology 1999; 140 (Suppl. 54): 18-23), published after the effective filing date of the present application, which is therefore not prior art, which supports Applicants assertion that high potency corticosteroids in combination with tazarotene have fewer side effects. The reference states "there was a trend towards a ***lower incidence of treatment-related adverse events as corticosteroid potency increased*** (from 42% with tazarotene plus placebo to 36%, 32%, and 31% with tazarotene plus the low-, mid-, and high potency corticosteroid, respectively)." The combination of the results presented in the present application and the teachings of the cited reference provide sufficient support for our conclusion that the presently claimed compositions have fewer side effects.

That a combination should be both more effective and have fewer side effects is certainly unexpected in any treatment program. The present

combination of a high potency corticosteroid and tazarotene produces a combination of higher efficacy and fewer side effects. Therefore, the present combination provides unexpected benefits which are not obvious to a person of ordinary skill in the art.

Based upon the reasoning presented herein, Applicant believes the claims are now patentable as they stand and respectfully requests that Examiner pass them to issue.

Respectfully submitted,



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CERTIFICATE OF EXPRESS MAIL UNDER 37 C.F.R. §1.10

I hereby certify that this Amendment and Reply and the documents referred to as enclosed herein are being deposited with the United States Postal Service on **DECEMBER 18, 2003** in an envelope as "Express Mail Post Office To Addressee" mailing label number EV193720739US with sufficient postage for Express Mail addressed to Mail Stop AF, Commissioner of Patents and Trademarks, P.O. Box 1450, Alexandria, VA 22313-1450.

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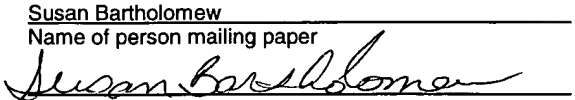

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Date: December 18, 2003